

**In the Specification:**

Please amend the specification as shown:

Please insert the following on page 1, before line 1:

**Sequence Listing**

**The instant application contains a Sequence Listing which has been submitted in ASCII format via EFS-Web and is hereby incorporated by reference in its entirety. Said ASCII copy, created on October 1, 2010, is named 21796.txt and is 212,512 bytes in size.**

Please delete the paragraph on page 9, lines 13-19 and replace it with the following paragraph:

**Fig. 1: Diagram of Dendritic cell (DC)-mediated analysis of tissue samples:**

Dendritic cells (DCs), the most specialized antigen-presenting cells (APCs), are brought in contact with an antigen source (e.g. synovial fluid) under optimal conditions for antigen uptake and antigen processing. As a control, DCs are cultured under the same conditions in the absence of synovial fluid antigens. After maturation of DCs, antigen-loaded MHC class II molecules are purified and the respective MHC class II-associated antigenic peptides are isolated and identified. **Fig. 1 discloses SEQ ID NOS 149-152, and 151, respectively, in order of appearance.**

Please delete the paragraph on page 9, lines 29-34 replace and it with the following paragraph:

**Fig. 2C: ION-TRAP MS/MS spectrum of the doubly charged peptide ion at m/z 977.1.**

The fragmentation masses, together with the mass of the parent ion, were searched against a non-redundant human database by using the SEQUEST algorithm. The retrieved sequence MPKNVVFVIDKSGSMSGR (one-letter-code) **(SEQ ID NO: 142)** corresponded to the dominant epitope ITIH4 (271-288) of the inter-alpha-trypsin inhibitor. The positions of the assigned series of N-terminal B-ions and C-terminal Y-ions are marked.

Please delete the paragraph on page 10, lines 1-8 and replace it with the following paragraph:

**Fig. 3:** Summary of the differential binding capacity of the tested candidate RA antigens in the context of binding to the *HLA-DRB1\*0401* allele. The putative *HLA-DRB1\*0401* binding motif is boxed in grey. and. As a measure for affinity, the peptide concentration was determined that was needed to reduce binding of a fixed amount of biotinylated HA(307-319) peptide by 50% (IC<sub>50</sub>) through competition. The reciprocal (1/ IC<sub>50</sub>) directly correlates with peptide affinity. As a reporter biotinylated HA(307-319) peptide from influenza hemagglutinin (Rothbard, J.B. et al., Cell 52 (1988) 515-523) was included in the study. **Fig. 3 discloses SEQ ID NOS 143, 1, 9, 15, 21, 26, 28, 35, 65, 68, and 72, respectively, in order of appearance.**

Please delete the paragraph on page 39, lines 1-3 and replace it with the following paragraph:

HA(307-319), PKYVKQNTLKLAT **(SEQ ID NO: 143)**, is an immunodominant epitope from influenza virus hemagglutinin that binds well to HLA-DR4 molecules and was used as a reporter peptide in an *in vitro* peptide binding assay (Rothbard, J.B. et al., Cell (1988) 52:515-523).

Please delete the paragraphs on page 41, line 24 to page 42, line 3 and replace them with the following paragraphs:

GILT is constitutively expressed in antigen-presenting cells, such as dendritic cells, macrophages and B cells, and facilitates unfolding of endocytosed antigens in MHC class II-containing compartments (MIIC) by enzymatically reducing disulfide bonds (Phan, U.T. et al., J Biol Chem 275 (2000) 25907-25914). Direct binding of GILT to HLA-DR molecules has been reported for B cells (Arunachalam, B. et al., J Immunol 160 (1998) 5797-5806). A rather long second epitope of GILT was found to bind to HLA-DR3 molecules: the 22-mer GILT (38-59) having the amino acid sequence SPLQALDFFGNGPPVNYKTGNL **(SEQ ID NO: 144)** (Chicz, R.M. et al., J Exp Med 178 (1993) 27-47).

In addition to GILT (192-207), another epitope of the same protein was identified in several RA samples, but also in control samples: GILT (210-227) with the amino acid sequence QPPHEYVPWVTVNGKPLE **(SEQ ID NO: 145)**. This epitope was accompanied by 3 other length variants: the 16-mer GILT (210-225), the 17-mer GILT (210-226) and the 19-mer GILT (210-228).

Please delete the paragraph on page 54, lines 14-21 and replace it with the following paragraph:

Interestingly, the analysis elucidated a second epitope of the same protein, which was highly abundant in all RA and control samples: the 16-mer SH3BGRL3 (29-44) with the amino acid sequence DGKRIQYQLVDISQDN **(SEQ ID NO: 146)**. In addition multiple length variants of the same epitope were found in most samples as well. As judged from the shortest length variant, SH3BGRL3 (31-42), the epitope contains almost similar *DRB1\*0401* anchor residues compared with SH3BGRL3 (15-26): 33I serves as a P1 anchor, 36Q as a P4 anchor and 38V as a P6 anchor (binding score -2). This similarity is reflected by comparable binding scores.

Please delete Table 1 and replace it with the following Table:

**Table 1: HLA-DR associated peptide antigens from serum and synovial fluid of patients with mostly non-erosive RA.**

| SEQ.<br>ID. NO. | RA-<br>type <sup>a</sup> | RF <sup>b</sup><br>(IU/ml) | Sample <sup>c</sup> | Haplo-<br>type <sup>d</sup> | Length | Sequence <sup>e</sup> | DRB1*0401-<br>binding<br>score <sup>f</sup> | Protein source <sup>g</sup>        |
|-----------------|--------------------------|----------------------------|---------------------|-----------------------------|--------|-----------------------|---|------------------------------------|
| 1               | N                        | -                          | S                   | 1                           | 14     | GDRGMQLMHANAQR        | 1%  | Interferon-gamma-                  |
| 2               | N                        | 6.8                        | S                   | 3                           | 17     | GDRGMQLMHANAQRTDA     |   | inducible lysosomal thiol          |
| 3               | N                        | 6.8                        | S                   | 3                           | 16     | GDRGMQLMHANAQRTD      |   | reductase                          |
| 2               | N                        | 9.1                        | Syn                 | 4                           | 17     | GDRGMQLMHANAQRTDA     |   | (192-205)                          |
| 3               | N                        | 9.1                        | Syn                 | 4                           | 16     | GDRGMQLMHANAQRTD      |   |                                    |
| 3               | E                        | 20.7                       | S                   | 3                           | 16     | GDRGMQLMHANAQRTD      |   |                                    |
| 58              | N                        | 9.1                        | Syn                 | 4                           | 17     | NIQPIFAVTSRMVKTYE     | 2%  | Integrin beta-2                    |
| 58              | N                        | 9.1                        | S                   | 4                           | 17     | NIQPIFAVTSRMVKTYE     |   | (315-331)                          |
| 59              | N                        | 9.1                        | S                   | 4                           | 19     | ENNIQPIFAVTSRMVKTYE   |   |                                    |
| 60              | N                        | 153                        | S                   | 5                           | 17     | NKVFGEDSVGVIFKNGD     | 3%  | Phosphatidylinositol-4,5-          |
| 60              | N                        | 88                         | S                   | 5                           | 17     | NKVFGEDSVGVIFKNGD     |   | bisphosphate 3-kinase<br>(792-808) |
| 61              | N                        | 9.1                        | S                   | 4                           | 16     | YPEQLKMTVVKLISHR      | 2%  | Urokinase-type                     |
| 61              | N                        | 9.1                        | Syn                 | 4                           | 16     | YPEQLKMTVVKLISHR      |   | plasminogen activator              |

|                   |                               |     |   |   |    |                                   |       |  |
|-------------------|-------------------------------|-----|---|---|----|-----------------------------------|-------|--|
|                   |                               |     |   |   |    |                                   |       | (328-343)  |
| 62                | N                             | 153 | S | 5 | 16 | KNTLYLQMNSLRAEDT                  | 1%    | Immunoglobulin heavy chain<br>V-III region (V <sub>H</sub> 26)<br>(95-110) |
| 62                | N                             | 88  | S | 5 | 16 | KNTLYLQMNSLRAEDT                  |       |  |
|                   |                               |     |   |   |    |                                   |       |  |
| 63                | N                             | 153 | S | 5 | 16 | NGGHYTYSENRVEKDG                  | 8%    | DJ-1 protein   |
| 63                | N                             | 88  | S | 5 | 16 | NGGHYTYSENRVEKDG                  |       | (135-150)  |
| <hr/>             |                               |     |   |   |    |                                   |       |  |
| <b><u>143</u></b> | strong HLA-DRB1*0401 binder   |     |   |   |    | PKYVKQNTLKLAT <sup>h (i)</sup>    | 1%    | Influenza Haemagglutinin<br>(307-319)                                      |
| <b><u>147</u></b> | moderate HLA-DRB1*0401 binder |     |   |   |    | KHKVYACEVTHQGLS <sup>h (ii)</sup> | 2%    | Immunoglobuline kappa<br>(188-202)   |
| <b><u>148</u></b> | weak HLA-DRB1*0401 binder     |     |   |   |    | KTIA YDEEARR <sup>h (iii)</sup>   | > 10% | <i>M. tuberculosis</i> Hsp65<br>(3-13)                                     |

<sup>a</sup>RA-type of the patient based on clinical diagnosis: persistent erosive (E) or persistent non-erosive (N) RA

<sup>b</sup>Rheumatoid factor

<sup>c</sup>Sample description: dendritic cells pulsed with serum (S) or synovial fluid (Syn)

<sup>d</sup>Haplotype of the buffy coat: (1) *HLA-DRB1\*0401, \*03011*; (2) *HLA-DRB1\*0401, \*0304*; (3) *HLA-DRB1\*0401, \*1301*; (4) *HLA-DRB1\*0401, \*0701*; (5) *HLA-DRB1\*0401, \*0407*

*\*0401, \*1301*; (4) *HLA-DRB1\*0401, \*0701*

<sup>e</sup>Sequences of the RA-derived peptides in one-letter-code. The *HLA-DRB1\*0401* binding motif is boxed in grey.

<sup>f</sup>Score of the epitope in context of the *HLA-DRB1\*0401* allele based on the TEPITOPE program (Hammer, J. et al., Adv Immunol 66 (1997) 67-100).

<sup>g</sup>Protein name according to the Swiss-Prot / TrEMBL database. The numbers in brackets represent the shortest length variant of the respective epitope.

<sup>h (i)</sup> Rothbard, J.B. et al., Cell 52 (1988) 515-523. <sup>h (ii)</sup> Chicz, R.M. et al., J Exp Med 178 (1993) 27-47. <sup>h (iii)</sup> van Schooten, W.C. et al., Eur J Immunol 19 (1989) 2075-2079.